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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|-----------------------|---------------------|------------------|
| 09/901,996 | 07/10/2001 | Francis Edward Dwulet | BMID 9809 US | 8740 |

7590

03/14/2003

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EXAMINER

WEBER, JON P

ART UNIT PAPER NUMBER

1651

DATE MAILED: 03/14/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------|-------------------------------|--|
| Office Action Summary | Application No. 09/901,996 | Applicant(s) DWULET ET AL. | |
| | Examiner Jon P Weber, Ph.D. | Art Unit 1651 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6</u> . | 6) <input type="checkbox"/> Other: _____ |

Status of the Claims

Claims 1-10 have been presented for examination.

Election/Restrictions

Applicant's election **without** traverse of claims 1-9 in Paper No. 9, filed 13 December 2002 is acknowledged. Claim 10 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. It is suggested that the nonelected claim be canceled in response to this Office action to expedite prosecution.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 at step (c) as well as claim 8 recite "eluting" which is confusing because this term is only used in connection with chromatography. There does not appear to be a chromatographic binding step preceding this step.

Claims 1 and 8-9 recite "modified enzyme" which is vague and indefinite because the nature and manner of the modification are unclear rendering the metes and bounds of the claim

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unclear. Is the modification a change in sequence, a chemical modification of a side chain, or substitution of an isotope, for example?

Regarding claim 6, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 7-8 recite the limitation "capture protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borjigin et al. (1993) in view of Altman et al. (1991), Roberts et al. (1992) and MacLennan et al. (US 6,326,155) and further in view of Conklin (US 6,380,354).

Borjigin et al. (1993) disclose forming fusion proteins with BPTI, binding the fusion protein to biotinylated trypsin or anhydrotrypsin, the complex is then purified on an avidin-agarose bead column. Near homogeneity was obtained (Figure 8). The BPTI-anhydrotrypsin tag system is suggested to be useful in protein purification, although BPTI derivatives with lower affinity would prove more useful when eluting from anhydrotrypsin (page 341, last paragraph).

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Borjigin et al. (1993) lacks explicitly cleaving the BPTI tag in the fusion protein after purifying the recombinant fusion protein to obtain the protein.

Altman et al. (1991) disclose forming fusion proteins with BPTI, binding the fusion protein to chymotrypsin immobilized on a solid support, cleaving and eluting the BPTI and its fusion partner, and finally purifying the BPTI (in this case they wanted the BPTI as opposed to the fusion partner).

Roberts et al. (1992) and MacLennan et al. (US 6,326,155) both disclose that using phage display libraries (with M13, for example), it is possible to engineer modified affinity binding ligands based upon naturally occurring protease inhibitors with more desirable properties or either increased or decreased affinity for the target enzyme. The target enzyme is used to screen the libraries for binding affinity under various conditions of temperature, pH, salt concentration or % volume of an organic cosolvent. Examples of target enzymes are elastase and tPA. At column 13, line 54 to column 14, line 10, MacLennan et al. (US 6,326,155) discusses a number of suitable stable inhibitor domains that are suitable candidates for this engineering, including, Kunitz.

Conklin (US 6,380,354) disclose that affinity tag peptides are widely used to purify or detect recombinant proteins. "In principle, any peptide or protein for which an antibody or other specific binding agent is available can be used as an affinity tag." (column 3, lines 42-44). A number of such affinity tags already in use are briefly described at column 3, lines 44-55.

A person of ordinary skill in the art at the time the invention was made would have been motivated to use the inhibitor peptide tags of Borjigin et al. (1993) and Altman et al. (1991) in the general process of purifying recombinant proteins because Conklin (US 6,380,354)

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especially indicate that any peptide with a specific binding agent can be used. The well-known procedures when the tags are other than peptide inhibitors always include steps of cleavage of the tag followed by separation of the tag and cleaving protease. The selection of a particular inhibitor-enzyme pair is an arbitrary matter of experimental design choice.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use enzyme inhibitors as affinity tags to purify recombinant proteins.

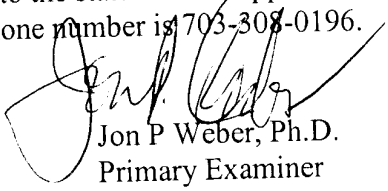
The prior art does not anticipate or reasonably suggest using the particular sequences as tags, nor does it anticipate or reasonably suggest the use of a psychrophilic enzyme.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
March 5, 2003